

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventor: Joseph RUBINFELD, et al.

Serial Number: 10/613,222

Filing Date: July 3, 2003

Title: RESTORING CANCER-SUPPRESSING
FUNCTIONS TO NEOPLASTIC CELLS
THROUGH DNA HYPOMETHYLATION

Group Art Unit: 1642

Examiner: Laura B. Goddard

CONFIRMATION NO: 7039

FILED ELECTRONICALLY ON: July 17, 2006

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria VA 22313-1450

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT
UNDER 37 CFR §1.97

Sir:

Applicants hereby submit an Information Disclosure Statement along with attached form PTO/SB/08. A copy of each listed publication is submitted, if required, pursuant to 37 CFR §§1.97-1.98, as indicated below.

Applicants respectfully request that the listed information be considered by the Examiner and be made of record in the above-identified application. Applicants further request that the Examiner initial and return the attached form PTO/SB/08 in accordance with MPEP §609.

Applicants reserve the right to establish the patentability of the claimed invention over any of the information provided herewith, and/or to prove that this information may not be prior art, and/or to prove that this information may not be enabling for the teachings purportedly offered.

This statement is not intended to represent that a search has been made or that the information cited in the statement is, or is considered to be, prior art or material to patentability as defined in §1.56.

- A. ☐ 37 CFR §1.97(b). This Information Disclosure Statement should be considered by the Office because:
- ☐ (1) It is being filed within 3 months of the filing date of a national application and is other than a continued prosecution application under §1.53(d);
-- OR --
 - ☐ (2) It is being filed within 3 months of entry of the national stage as set forth in §1.491 in an international application;
-- OR --
 - ☐ (3) It is being filed before the mailing of a first Office action on the merits;
-- OR --
 - ☐ (4) It is being filed before the mailing of a first Office action after the filing of a request for continued examination under §1.114.
- B. ☒ 37 CFR §1.97(c). Although this Information Disclosure Statement is being filed after the period specified in 37 CFR §1.97(b), above, it is filed before the mailing date of the earlier of (1) a final office action under §1.113, (2) a notice of allowance under §1.311, or (3) an action that otherwise closes prosecution on the merits, this Information Disclosure Statement should be considered because it is accompanied by one of:
- ☐ a statement as specified in §1.97(e) provided concurrently herewith;
-- OR --
 - ☒ a fee of \$180.00 as set forth in §1.17(p) authorized below, enclosed, or included with the payment of other papers filed together with this statement.
- C. ☐ 37 CFR §1.97(d). Although this Information Disclosure Statement is being filed after the mailing date of the earlier of (1) a final office action under §1.113 or (2) a notice of allowance under §1.311, it is being filed before payment of the issue fee and should be considered because it is accompanied by:
- i. a statement as specified in §1.97(e);
-- AND --
 - ii. a fee of \$180.00 as set forth in §1.17(p) is authorized below, enclosed, or included with the payment of other papers filed together with this Statement.
- D. ☐ 37 CFR §1.97(e). Statement.
- ☐ A statement is provided herewith to satisfy the requirement under 37 CFR §§1.97(c);
-- AND/OR --
 - ☐ A statement is provided herewith to satisfy the requirement under 37 CFR §§1.97(d);
-- AND/OR --
 - ☐ A copy of a dated communication from a foreign patent office clearly showing that the information disclosure statement is being submitted within 3 months of the filing date on the communication is provided in lieu of a statement under 37 C.F.R. § 1.97(e)(1) as provided for under MPEP 609.04(b) V.
- E. ☐ Statement Under 37 C.F.R. §1.704(d). Each item of information contained in the information disclosure statement was first cited in a communication from a foreign patent office in a counterpart application that was received by an individual designated in § 1.56(c) not more than thirty (30) days prior to the filing of this information disclosure statement. This statement is made pursuant to the

requirements of 37 C.F.R. § 1.704(d) to avoid reduction of the period of adjustment of the patent term for Applicant(s) delay.

F. ☒ 37 CFR §1.98(a)(2). The content of the Information Disclosure Statement is as follows:

- ☐ Copies of each of the references listed on the attached Form PTO/SB/08 are enclosed herewith.

-- OR --

- ☒ Copies of U.S. Patent Documents (issued patents and patent publications) listed on the attached Form PTO/SB/08 are NOT enclosed.

-- AND/OR --

- ☒ Copies of Foreign Patent Documents and/or Non Patent Literature Documents listed on the attached Form PTO/SB/08 are enclosed in accordance with 37 CFR §1.98 (a)(2).

-- AND/OR --

- ☐ Copies of pending unpublished U.S. patent applications are enclosed in accordance with 37 CFR §1.98(a)(2)(iii).

G. ☐ 37 CFR §1.98(a)(3). The Information Disclosure Statement includes non-English patents and/or references.

- ☐ Pursuant to 37 CFR §1.98(a)(3)(i), a concise explanation of the relevance of each patent, publication or other information provided that is not in English is provided herewith.

- ☐ Pursuant to MPEP 609(B), an English language copy of a foreign search report is submitted herewith to satisfy the requirement for a concise explanation where non-English language information is cited in the search report.

-- OR --

- ☐ A concise explanation of the relevance of each patent, publication or other information provided that is not in English is as follows: _____

- ☐ Pursuant to 37 CFR §1.98(a)(3)(ii), a copy of a translation, or a portion thereof, of the non-English language reference(s) is provided herewith.

H. ☐ 37 CFR §1.98(d). Copies of patents, publications and pending U.S. patent applications, or other information specified in 37 C.F.R. § 1.98(a) are not provided herewith because:

- ☐ Pursuant to 37 CFR §1.98(d)(1) the information was previously submitted in an Information Disclosure Statement for another application under which this application claims priority for an earlier effective filing date under 35 U.S.C. 120.

Application in which the information was submitted: _____

Information Disclosure Statement(s) filed on: _____

AND

- ☐ The information disclosure statement submitted in the earlier application complied with paragraphs (a) through (c) of 37 CFR §1.98.

- I. ☒ *Fee Authorization.* The Commissioner is hereby authorized to charge the above-referenced fees of \$180.00 and charge any additional fees or credit any overpayment associated with this communication to Deposit Account No. 23-2415 (Docket No.12636-330.201).

Respectfully submitted,

WILSON SONSINI GOODRICH & ROSATI

Dated: July 14, 2006

650 Page Mill Road
Palo Alto, CA 94304-1050
(650) 493-9300
Customer No. 021971

By: 

Shirley Chen, Reg. No. 44,608

Under the paperwork Reduction Act of 1995, no persons required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(Use as many sheets as necessary)</i>			Complete if Known		
			Application Number	10/613,222	
			Filing Date	July 3, 2003	
			First Named Inventor	Joseph Rubinfeld	
			Art Unit	1642	
			Examiner Name	Laura B. Goddard	
Sheet	1	Of	4	Attorney Docket Number	12636-330.201

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No.	Document Number Number-Kind Code ² (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		US-2004/0109846	6/10/2004	Rubinfeld et al.	

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No.	Foreign Patent Document Country Code ² - Number ² - Kind Code ² (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ³

Examiner Signature	Date Considered
--------------------	-----------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ²Applicant's unique citation designation number (optional). ³See Kind Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ⁴Best Office that issued the document, by the two-letter code (WIPO Standard ST 3). ⁵For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁶Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST 16 if possible. ⁷Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22315-1452. DO NOT SEND FILES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22315-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

Under the paperwork Reduction Act of 1995, no persons required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(Use as many sheets as necessary)</i>			Complete if Known		
			Application Number	10/613,222	
			Filing Date	July 3, 2003	
			First Named Inventor	Joseph Rubinfeld	
			Art Unit	1642	
			Examiner Name	Laura B. Goddard	
Sheet	2	Of	4	Attorney Docket Number	12636-330.201

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ⁴
		BOUCHARD, et al. Incorporation of 5-Aza-2'-deoxycytidine-5'-triphosphate into DNA. Interactions with mammalian DNA polymerase alpha and DNA methylase. Mol. Pharmacol. 1983; 24:109-114.	
		BOVENZI, et al. DNA methylation of retinoic acid receptor beta in breast cancer and possible therapeutic role of 5-aza-2'-deoxycytidine. Anticancer Drugs. 1999;10:471-476.	
		CALIARO, et al. Response of four human ovarian carcinoma cell lines to all-trans retinoic acid: relationship with induction of differentiation and retinoic acid receptor expression. Int. J. Cancer 1994;56:743-748.	
		COTE, et al. Demethylation by 5-aza-2'-deoxycytidine of specific 5-methylcytosine sites in the promoter region of the retinoic acid receptor beta gene in human colon carcinoma cells. Anti-Cancer Drugs. 1998;9:743-750.	
		CROWE, D. L. Retinoic acid receptor beta induces terminal differentiation of squamous cell carcinoma lines in the absence of cyclin-dependent kinase inhibitor expression. Cancer Res. 1998;58:142-148.	
		DENG, et al. Loss of heterozygosity in normal tissue adjacent to breast carcinomas. Science. 1996; 274:2057-2059.	
		DENISSENKO, et al. Cytosine methylation determines hot spots of DNA damage in the human P53 gene. Proc. Natl. Acad. Sci. USA 1997; 94:3893-3898.	
		EHRlich, et al. Amount and distribution of 5-methylcytosine in human DNA from different types of tissues of cells. Nucleic Acid Res. 1982; 10:2709-2721.	
		HAMEL, et al. G1 cyclins and control of the cell division cycle in normal and transformed cells. Cancer Invest. 1997;15:143-152.	
		HERMAN, et al. Inactivation of the CDKN2/p16/MTS1 gene is frequently associated with aberrant DNA methylation in all common human cancers. Cancer Res. 1995;55:4525-4530.	

Examiner Signature	Date Considered
--------------------	-----------------

*EXAMINER: Initial if reference considered, whether or not citation is in accordance with MPEP 608. Draw line through citation if not in accordance and not considered. Include copy of this form with each communication to applicant. ¹Applicant's unique citation designation number (optional). ²See kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST 3). ⁴For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST 16 if possible. ⁶Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. This information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-6100 (1-800-766-9100) and select option 2.

Under the paperwork Reduction Act of 1995, no persons required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(Use as many sheets as necessary)</i>				Complete if Known	
				Application Number	10/613,222
				Filing Date	July 3, 2003
				First Named Inventor	Joseph Rubinfeld
				Art Unit	1642
				Examiner Name	Laura B. Goddard
Sheet	3	Of	4	Attorney Docket Number	12636-330.201

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ⁶
		HOULE, et al. Tumor-suppressive effect of the retinoic acid receptor beta in human epidermoid lung cancer cells. Proc. Natl. Acad. Sci. USA. 1993;90:985-989.	
		ISSA, et al. Increased cytosine DNA-methyltransferase activity during colon cancer progression. J. Natl. Cancer Inst. 1993;85:1235-1240.	
		JONES, et al. Cellular differentiation, cytidine analogs and DNA methylation. Cell. 1980;20:85-93.	
		JUTTERMANN, et al. Toxicity of 5-aza-2'-deoxycytidine to mammalian cells is mediated primarily by covalent trapping of DNA methyltransferase rather than DNA demethylation. Proc. Natl. Acad. Sci. USA 1994;91:11797-11801.	
		KANE, et al. Methylation of the hMLH1 promoter correlates with lack of expression of hMLH1 in sporadic colon tumors and mismatch repair-defective human tumor cell lines. Cancer Res. 1997;57:808-811.	
		KISSINGER, et al. Determination of the antileukemia agents cytarabine and azacitidine and their respective degradation products by high-performance liquid chromatography. J. Chromat. 1986; 353:309-318.	
		MODRICH, et al. Mismatch repair in replication fidelity, genetic recombination, and cancer biology. Annu. Rev. Biochem. 1996; 65:101-133.	
		MOJAVERIAN, et al. Development of an intravenous formulation for the unstable investigational cytotoxic nucleosides 5-azacytosine arabinoside (NSC 281272) and 5-azacytidine (NSC 102816). J. Pharm. Pharmacol. 1984;36:728-733.	
		MOMPARLER, R. L. Molecular, cellular and animal pharmacology of 5-aza-2'-deoxycytidine. Pharmacol Ther. 1985;30:287-99.	
		OTTAVIANO, et al. Methylation of the estrogen receptor gene CpG island marks loss of estrogen receptor expression in human breast cancer cells. Cancer Res. 1994; 54:2552-2555.	

Examiner Signature	Date Considered
--------------------	-----------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹Applicant's unique citation designator number (optional). ²See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST 3). ⁴For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST 16 if possible. ⁶Applicant is to place a check mark here if English language translation is attached.

This collection of information is required by 37 CFR 1.57 and 1.58. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22311-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-0199 (1-800-766-9199) and select option 2.

Under the paperwork Reduction Act of 1995, no person required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

Complete if Known

Application Number	10/613,222
Filing Date	July 3, 2003
First Named Inventor	Joseph Rubinfeld
Art Unit	1642
Examiner Name	Laura B. Goddard
Attorney Docket Number	12636-330.201

Sheet

4

Of

4

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ⁴
		OTTERSON, et al. CDKN2 gene silencing in lung cancer by DNA hypermethylation and kinetics of p16INK4 protein induction by 5-aza 2'deoxyctidine. <i>Oncogene</i> 1995;11:1211-1216.	
		POMPON, et al. Reversed-phase high-performance liquid chromatography of nucleoside analogues. Simultaneous analysis of anomeris D-xylo- and D-lyxofuranonucleosides and some other D-pentofuranonucleosides. <i>J. Chromat.</i> 1987; 388:113-122.	
		ROODI, et al. Estrogen receptor gene analysis in estrogen receptor-positive and receptor-negative primary breast cancer. <i>J. Natl. Cancer Inst.</i> 1995;87:446-451.	
		SHEN, et al. The rate of hydrolytic deamination of 5-methylcytosine in double-stranded DNA. <i>Nucleic Acid Res.</i> 1994;22:972-976.	
		SWISSELM, et al. Down-regulation of retinoic acid receptor beta in mammary carcinoma cell lines and its up-regulation in senescent normal mammary epithelial cells. <i>Cell Growth Differ.</i> 1994;5:133-141.	
		YEVIN, et al. Gene methylation patterns and expression (in DNA Methylation: Molecular Biology and Biological Significance. 1993. Basel: Birkhauser Verlag). EXS. 1993;64:523-568.	

Examiner Signature	Date Considered
--------------------	-----------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹Applicant's unique citation designation number (optional). ²See Kinda Codes of USPTO Patent Documents at www.uspto.gov at MPEP 901.04. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁶Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1458, Alexandria, VA 22313-1458.

If you need assistance in completing the form, call 1-800-PTO-0199 (1-800-796-9199) and select option 2.